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(54) **Disinfecting and cleaning composition.**

(57) A rapid disinfecting formulation for ophthalmic devices, i.e. contact lenses inter alia, is disclosed. The formulations comprise a combination of a C₃₋₈alkylene glycol, an ophthalmically acceptable surfactant, a lower alkanol, water, and optionally a pH regulator, a tonicity enhancer, and a viscosity enhancer. The method comprises contacting the ophthalmic device to be disinfected with the above formulation, physically rubbing the device surface with the formulation, and rinsing the so treated device to remove remaining residue.

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RAPID OPHTHALMIC DEVICE DISINFECTING SOLUTION AND METHOD

The present invention relates to the field of contact lens disinfection systems, especially solutions and suspensions, although it can be applied to any disinfection purpose where the system components are compatible with the materials being disinfected.

Cleaning regimens for ophthalmic devices of various types differ significantly in the cleaning efficacy and their procedural complexity. The typical regimens are heat disinfection and chemical (i.e. cold) disinfection, which eliminate pathogens and enzymatic cleaning to remove stubbornly adhering protein. Loosely held proteins and other loosely held contaminants can typically be removed by rubbing alone.

While various combinations of these regimens are indicated for various types of contact lenses, frequently contact lens users are less than diligent, and sometimes downright negligent in their strict adherence to the recommended procedures. Hence, a simplified system for disinfection and general cleaning of contact lenses has been long sought after.

Additionally, many disinfection systems currently known are not compatible with a large number of different types of lenses. It has been observed that there is a great deal of consumer confusion, especially when brand loyalty is being sacrificed for price. While many system/lens combinations may be suitable, others may result in irreversibly fouling the lens requiring that it be discarded and a new lens purchased. Therefore, it has also been desirable to develop a single disinfection and cleaning system which is compatible with most, if not all, contact lens materials.

Still further, most known disinfection systems require substantial amounts of time to achieve the desired degree of disinfection. Many times, contact lens wearers, for whatever the reason, neglect to continue the regimen for a period sufficient to disinfect the lens properly. Therefore, it is essential to proper compliance that a very rapid disinfection system for contact lenses be developed.

Exemplary known disinfection systems include those disclosed in British Patents 2,003,033 and 1,472,084; and US Patents 4,525,346 and 4,127,423. Typical marketed cleaning and disinfection systems are Cooper Vision's Miraflex® and Alcon's Preflex®/Polyclens®/Polyflex® systems. However, each of these suffers from one or more of the problems set out above.

It is an object of the invention to provide an ophthalmic device, preferably contact lens, disinfection system which has a simple regimen. It is a further object of the invention to provide a disinfection system for ophthalmic devices which can be completed in a short time period, typically in a couple of minutes or less. It is another object of the invention to provide solutions to achieve the foregoing objects.

Still another object is to provide a solution and method for cleaning contact lenses, which, with minimal patient input, both cleans and disinfects the contact lenses.

It is yet another object of the invention to provide a solution for cleaning and disinfecting contact lenses which is compatible with a wide range of contact lens types.

A further object of the invention is to provide a cleaning and disinfection system for ophthalmic devices which can be easily utilized by the eye-care professional to clean and disinfect such devices between usages in successive examinations.

These and other important objects are realized by a disinfection and cleaning formulation for ophthalmic devices, preferably contact lenses, comprising:

- a) a C₃₋₈alkylene glycol;
- b) an ocularly acceptable, ophthalmic device material compatible, surfactant;
- c) a lower alkanol;
- d) optionally a pH regulating agent;
- e) optionally a tonicity builder;
- f) optionally a viscosity builder; and
- g) water.

The formulation of the invention both disinfects and cleans contact lenses and other ophthalmic device materials in a very short period of time; typically under three minutes.

The formulations within the invention can also be used in virtually any composition requiring rapid disinfection, low toxicity and low irritancy. While not limiting the scope of the composition utility, exemplary utilities include inclusion of the invention composition within: topical medical preparations, cosmetics, facial cleansers, disinfecting soaps such as surgical soaps, disinfecting shampoos and disinfecting cleaners for household and/or industrial use. The only limitation on the incorporation of the instant formulation in various products or using them for various purposes is that the ingredients of the present invention be compatible with the ingredients of the composition to which it is to be added as well as with the surfaces to which it will be applied.

The instant invention is a formulation, preferably a hypertonic solution or suspension, more preferably a solution, which is primarily a cleaner of proteins and debris and both cleans and disinfects ophthalmic device materials, especially contact lenses, in a relatively short period of time; i.e. under about three minutes, preferably under about 1.5 minutes, more preferably under about one minute, still more preferably in about 20 to about 40 seconds, most preferably in about 30 seconds. The formulation will usually be of the following composition, but the fourth, fifth and sixth components are only optional:

- a) about 10 % by weight to about 50 % by weight of a C₃₋₈alkylene glycol;
- b) about 0.5 % to about 25 % by weight of a compatible surfactant;
- c) about 2 % to about 50 % by weight of a lower alkanol;
- 10 d) 0 to about 2 % by weight of a pH adjusting or regulating agent;
- e) 0 up to an amount of a tonicity builder sufficient to raise the solution tonicity to less than the equivalent of a 5 % by weight NaCl solution;
- f) 0 to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent;
- and
- 15 g) the balance of a suitable solvent which is preferably water.

In a preferred composition the surfactant is present from about 2 % to about 15 % by weight and the lower alkanol is present from about 2 % to about 30 % by weight.

Without being bound to the theory presented, it is believed that the various components work in tandem so that cleaning and disinfecting is completed in a minimal amount of time. The glycol has a disinfectant property and a polymeric swelling property. The swelling which results partially cracks any encrustations on the surface and allows the formulation to better reach the subsurface area of the material being disinfected thereby allowing for better disinfection and cleaning. The surfactant is primarily a cleaner of proteins. However, it has a slight antimicrobial contribution, especially when a quaternary amine is present at a low pH. The lower alkanol has an antimicrobial effect of its own. The pH regulator is present so as to avoid deleterious pH changes due to the other components and conditions of use to which one puts the invention. The tonicity builder is present to ensure that the tonicity of the solution is hypertonic. Hypertonicity has an antimicrobial effect on its own, and additionally, prevents the material which is being disinfected from excessively swelling. The viscosity builder is really present for aesthetic purposes and to more easily carry out the first step, i.e. rubbing the device surface with the formulation. The water, of course, is present as an ophthalmically acceptable carrier for all of the other components.

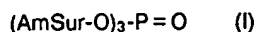
The invention method is a regimen of rubbing a few drops of the formulation on the surface of the device and one rubs it for 5-30 seconds on each surface. The device is then preferably rinsed for at least 5 seconds with normal saline and stored in normal saline for at least 20 seconds, after which the device can be reused. When used as part of other non-ophthalmic device cleaning compositions, the composition of the instant invention is incorporated into an appropriate formulation as set forth above and applied in the normal course to a normal surface for that type of formulation. Slight rubbing of the formulation on the surface may be employed, but may not be necessary depending upon the performance of the formulation's other ingredients. After application and optional rubbing, rinsing with saline (if tonicity need be maintained) or water (if tonicity is not critical) completes the operation. Where the instant formulation is used alone, it is applied in the normal manner as any other cleaner or disinfectant to the compatible surface, rubbed slightly for 5-30 seconds and rinsed with normal saline or water as appropriate for the purpose for which the composition is being used.

In the typical formulation of the invention, the C₃₋₈alkylene glycol is present from about 10 % to about 50 % by weight, preferably about 15 % to about 40 % by weight, still more preferably about 17 % to about 25 % by weight, most preferably about 21 % by weight of the entire formulation.

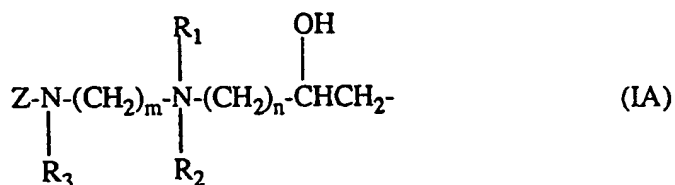
The C₃₋₈alkylene glycol is preferably selected from 1,2 or alpha,omega glycols such as 1,2-propylene glycol, 1,2-butylene glycol, 1,2-pentylene glycol, 1,2-hexylene glycol, 1,3-propylene glycol, 1,4-butylene glycol, 1,5-pentylene glycol, and 1,6-hexylene glycol. Also preferably, the C₃₋₈alkylene glycols are C₃ or C₄ alkylene glycols such as 1,2-propylene glycol, 1,3-propylene glycol, 1,2-butylene glycol, 1,3-butylene glycol, 1,4-butylene glycol, 2,3-butylene glycol, 2-methyl-1,2-propylene glycol, and 2-methyl-1,3-propylene glycol. Most preferably, the C₃₋₈alkylene glycol is 1,2-propylene glycol or 1,3-propylene glycol. 1,6-Hexylene glycol is also preferred.

The surfactant is present in an amount of about 0.5 % to about 25 % by weight, but usually about 2 % to about 15 % by weight, preferably about 3 % to about 12 % by weight, most preferably about 5 % by weight to about 10 % by weight of the entire formulation. The surfactant is selected from virtually any ocularly acceptable surfactant including non-ionic, anionic, and amphoteric surfactants, but is preferably selected from

ba) compounds of formula I

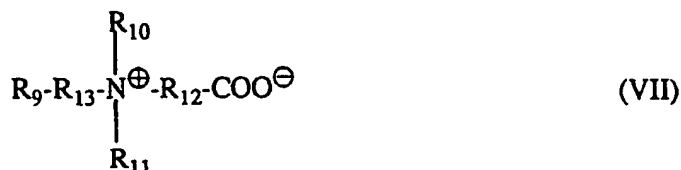


wherein the group AmSur is of the formula



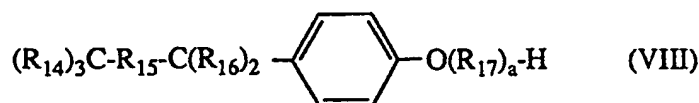
wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R_1 and R_2 is a carbon substituted by C_{5-17} alkyl; and n and m are each independently 1 to 4. Where AmSur contains a net charge, a suitable ocularly acceptable counter ion, such as a halogenide, e.g. chloride, is also present in an appropriate amount. The three AmSur radicals can be the same or different, but preferably all three AmSur radicals in one molecule are the same;

bb) compounds of the formula

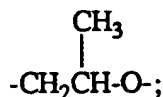


wherein R_9 is alkyl of 5-17 carbon atoms or a C_{6-20} alkanoylamino; each of R_{10} and R_{11} is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R_{12} is an alpha,omega-alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R_{13} is alpha,omega- C_{1-8} alkylene;

bc) compounds of the formula



wherein each R_{14} and each R_{16} is independently C_{1-4} alkyl; R_{15} is C_{1-4} -alpha,omega-alkylene; each R_{17} is independently $-\text{CH}_2\text{CH}_2\text{O}-$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-$, or



and a is 3-18; and

bd) compounds of the formula

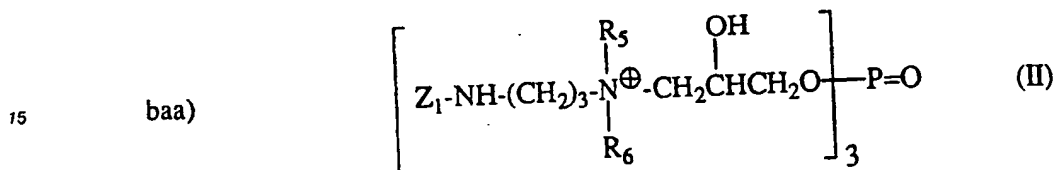


wherein B is a C_{1-4} alpha,omega-alkylene; p is an integer from 0 to (d-1); b is an integer which is (d-p-1); d is 4 to 7; each R_{18} is independently H or a C_{1-4} alkyl which is unsubstituted or substituted by at least one

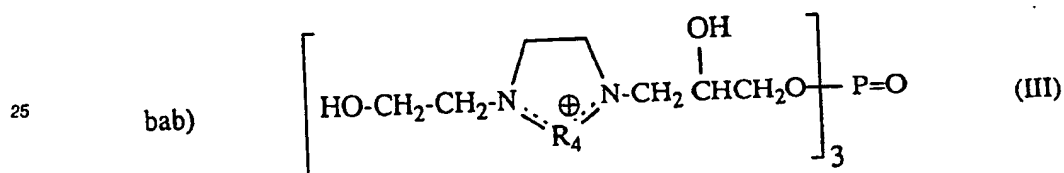
R_{19} ; each R_{19} is independently hydroxy which is free, etherified by R_{20} , or esterified by R_{21} ; each R_{20} is a C_{2-4} straight or branched oxyalkylene or poly(C_{2-4} straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21} ; and each R_{21} is independently an acyl of a C_{2-24} alkanolic acid or a C_{4-24} alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group. Compounds of formula VII are typically available from Miranol under the names Mirataine® and Miranol®; compounds of formula VIII are available under the names Igepal CA®, Polytergent® and Triton X®; and compounds of formula IX are available under the Span® and Tween® brand names.

Hereinafter and hereinafter "lower", such as in lower alkyl, refers to residues having up to 7 carbon atoms, preferably up to 4 carbon atoms.

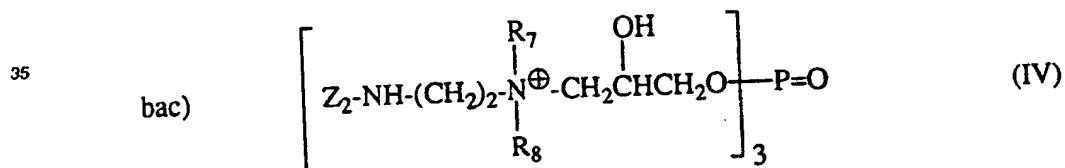
Preferably the compounds of formula I are selected from



20 wherein R_5 and R_6 are each C_{1-4} alkyl and Z_1 is C_{6-18} alkanoyl;



30 wherein R_4 is a carbon substituted by C_{5-17} alkyl and the dotted lines indicate that there is one double bond between R_4 and one of the nitrogens attached to R_4 ; and

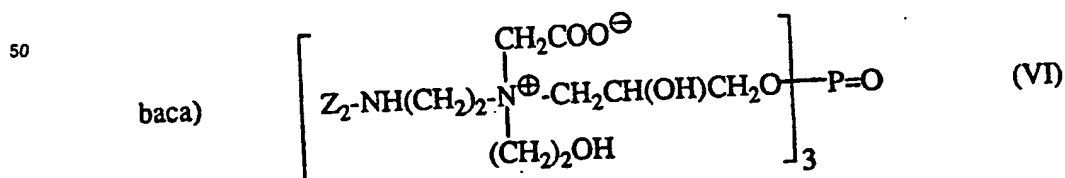


40 wherein Z_2 is C_{12-14} alkanoyl, one of R_7 and R_8 is carboxy lower alkyl, and the other of R_7 and R_8 is hydroxy lower alkyl.

Compounds of formulae II-IV are available from Mona Industries, New Jersey under the series trade name Monaquat®-P. More preferably, within formulae II-IV, are the compounds

45 baaa) $[Z_1-NH-(CH_2)_3-N^{\oplus}(CH_3)_2-CH_2-CH(OH)-CH_2-O]_3-P=O \cdot 3Cl^{\ominus}$ (V) wherein Z_1 is C_{6-17} alkanoyl (available under the name Monaquat® P-TC) or C_{12-14} alkanoyl (available under the name Monaquat® P-TD);

baba) compounds of formula III, available under the name Monaquat® P-TZ; and



wherein Z_2 is C_{12-14} alkanoyl, available under the name Monaquat® P-TL. The most preferable compound of

the Monaquat®P series for use in the instant invention is Monaquat®P-TL, i.e. compounds of formula VI. Compounds within formula II generally are disclosed in US Patents 4,209,449 and 4,336,385, the disclosures of which are included herein by reference.

Another preferred class of surfactants includes poloxamers, reverse poloxamers, meroxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycolbuteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, cetareths, NTA-salts, EDTA salts, and pentetate salts. Within this group, especially useful are:

poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 288, 331, 333, 334, 335, 338, 401, 402, 403, and 407;

meroxapols 105, 108, 171, 172, 174, 178, 251, 252, 254, 255, 258, 311, 312, and 314;

poloxamines 304, 504, 701, 702, 704, 707, 901, 904, 908, 1101, 1102, 1104, 1107, 1301, 1302, 1304, 1307, 1501, 1502, 1504, and 1508;

polyethylene glycols selected from PEGs 4, 6, 8, 12, 20, 32, 40, 75, 150, and PEG 6 methyl ether;

polypropylene glycols selected from PPGs 9, 12, 17, 26, and 30;

polypropylene glycol-buteths selected from ppg-5-buteth-7, ppg-7-buteth-10, ppg-12-buteth-16, ppg-20-buteth-30, ppg-28-buteth-35, and ppg-33-buteth-45;

ppg-26-oleate;

ppg-6-pareth;

tetrahydroxypropylethylenediamine;

cetareth 27 and 55;

trisodium NTA;

trisodium EDTA and tetrasodium EDTA;

EDTA; and

pentasodium pentetate. Each of these compounds can be found in the C.T.F.A. Ingredient Dictionary.

The lower alkanol is present from about 2 % to about 50 % by weight, but usually from about 2 % to about 30 % by weight, preferably from about 10 % to about 20 % by weight, most preferably about 16 % by weight of the entire formulation. Lower alkanol is selected from C₁₋₇, preferably C₁₋₄, straight or branched alkanols, such as methanol, ethanol, n-propanol, isopropanol, n-butanol, sec-butanol and t-butanol, more preferably isopropanol or ethanol, most preferably isopropanol.

The pH regulating component, when present, can be added as a preformed buffer or can be formed in situ. If the pH of the solution without this component is suitable it is not required, although its presence is desirable. Any ocularly compatible inorganic or organic acid or base or buffer system can be used. Typical buffer systems include the well known phosphate or borate systems. Other suitable organic buffer systems include, without limitation, the lactate, pyruvate, citrate, tartrate, acetate, and laurate systems.

The pH of the final solution may be advantageously in the range of 3 to 7.0, preferably 5 to 7, more preferably about 5.5 to about 6. The lower pHs, while suitable, are advantageous in that minimum disinfecting time is shortened over the same composition at higher pH, but disadvantageous in that reestablishment of neutral pH is necessary before a lens is placed back on the eye.

Most preferably the buffer system used will have a pK in the range of the desired pH range so as to maximize the buffering capacity. The most preferable buffer system is lactic acid/lactate which is preferably formed in situ by the addition of lactic acid alone. In the case of lactic acid/lactate as the pH adjuster (i.e. buffer), the combined lactic acid and lactate are preferably present from about 0.5 to about 2 % by weight of the solution based on lactate ion, more preferably about 0.75 % to about 1.5 %, most preferably about 1.1 % of the solution.

The tonicity builder, when present, is typically present in an amount which yields a tonicity for the invention solution equivalent to sodium chloride solutions in the range of 0.5 up to but less than 5 % sodium chloride, preferably up to 2 % sodium chloride, still more preferably in the range of 0.75 to 1.5 % sodium chloride, more preferably about 0.9 to 1.1 % sodium chloride, most preferably about 1 % sodium chloride, all percentages being w/v. The most preferable compound for use as a tonicity builder is sodium chloride, although any ocularly compatible inorganic or organic salt which does not interfere with the other components will do. For example, excess lactic acid and lactate salt may be used to enhance the buffering capacity and simultaneously contribute sufficiently to the tonicity that a tonicity builder is not necessary or desired. Hence, the tonicity builder can be absent entirely or present up to an amount equivalent in tonicity with just under 5 % sodium chloride.

The overall solution tonicity should preferably be hypertonic, preferably at least equivalent to 1.1 % NaCl. It should not be less than isotonic. The tonicity builder amounts stated above can be adjusted by those of ordinary skill to have the solution meet these overall more preferable limits. Typical tonicity builders include ophthalmically acceptable alkaline metal or alkaline earth metal halide, phosphate, car-

bonate, sulfate, etc.

The viscosity enhancer, when present, is present to help increase the solution viscosity to preferably not greater than 100 cps, more preferably not greater than 80 cps, still more preferably not greater than 30 cps, most preferably not greater than 10 cps. Any ocularly compatible non-ionic or quaternary ammonium viscosity enhancer is suitable. Examples of non-ionic viscosity enhancers utilizable on the instant invention include: lower alkyl celluloses (i.e. methyl cellulose, ethyl cellulose, etc.) hydroxy lower alkyl celluloses (i.e. hydroxy methyl cellulose, hydroxy ethyl cellulose, hydroxy propyl cellulose, etc.), poloxamers, reverse poloxamers, ethoxylated ethylene diamines, etc.

Preferably, the viscosity enhancer is a cellulose ether, more preferably hydroxy lower alkyl cellulose, most preferably hydroxy ethyl cellulose, such as HECQP 4400 available from Union Carbide. In a most preferred solution, hydroxy ethyl cellulose is the viscosity enhancer and is present an amount of about 0.1 % by weight of the solution.

Another preferred class of viscosity enhancing agents includes poloxamers, reverse poloxamers, merxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, cetareths, NTA-salts, EDTA salts, and pentetate salts. Within this group, especially useful are:

poloxamers 101, 105, 108, 122, 123, 124, 181, 182, 183, 184, 185, 188, 212, 215, 217, 231, 234, 235, 237, 238, 282, 288, 331, 333, 334, 335, 338, 401, 402, 403, and 407;

merxapols 105, 108, 171, 172, 174, 178, 251, 252, 254, 255, 258, 311, 312, and 314;

poloxamines 304, 504, 701, 702, 704, 707, 901, 904, 908, 1101, 1102, 1104, 1107, 1301, 1302, 1304, 1307, 1501, 1502, 1504, and 1508;

polyethylene glycols selected from PEGs 4, 6, 8, 12, 20, 32, 40, 75, 150, and PEG 6 methyl ether;

polypropylene glycols selected from PPGs 9, 12, 17, 26, and 30;

polypropylene glycol-buteths selected from ppg-5-buteth-7, ppg-7-buteth-10, ppg-12-buteth-16, ppg-20-buteth-30, ppg-28-buteth-35, and ppg-33-buteth-45;

ppg-26-oleate;

ppg-6-pareth;

tetrahydroxypropylethylenediamine;

cetareth 27 and 55;

trisodium NTA;

trisodium EDTA and tetrasodium EDTA;

EDTA; and

pentasodium pentetate. Each of these compounds can be found in the C.T.F.A. Ingredient Dictionary.

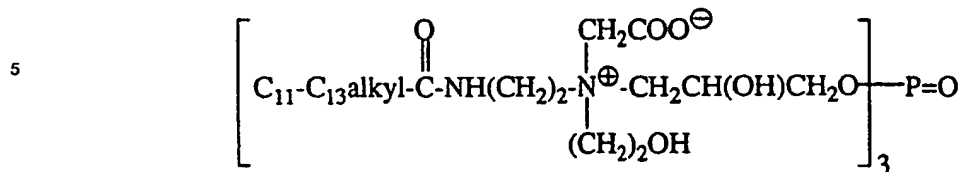
The solution of the invention can be formulated from the above components in any manner known in the art. For example the solid components can be dissolved directly in the water, either simultaneously or sequentially, with liquid components being added thereto either before or after the solid components. Alternatively the solid components can be triturated with one or more non-water liquid components and this mixture diluted with an appropriate amount of water. It is preferable to dissolve all of the components (other than the viscosity enhancer) first and then mix the viscosity enhancer into this solution. Variations of the above will be apparent to the ordinarily skilled formulator.

The instant solutions are rapid cleaning and disinfecting solutions for a wide range of contact lens and other materials. Typically, one applies a few drops of the solution to the lens material and rubs it for 5 to 30 seconds, preferably 10 to 20 seconds, more preferably about 15 seconds. This is repeated for the opposite surface. The lens is then rinsed in normal saline for at least 5 seconds, preferably 10 to 20 seconds, most preferably 15 seconds, and stored in normal saline for at least 20 seconds, preferably 30 seconds to 1.5 minutes, most preferably about 1 minute. Longer storing times are acceptable, but not necessary. The instant solution can be used in the above method for all types of contact lenses; soft lenses, hard lenses, and rigid gas permeable lenses. Such lens materials for which the instant solution can be used include bufilcon A, cabufocon A, crofilcon A, deltafilcon A, deltafilcon B, dimefilcon A, droxifilcon, etafilcon A, hefilcon A, hefilcon B, itafocon A, lidofilcon A, mafilcon A, ocufilcon A, ocufilcon B, optacryl 60, pasifocon A, pasifocon B, pasifocon C, perfilcon A, phemfilcon A, polymacon, porofocon B, silafilcon A, silafocon A, tefilcon, tetrafilcon A, vifilcon A, PMMA, silicone/MMA copolymer, MMA/glycerol methacrylate copolymer, and poly t-butyl styrene. Others will be apparent to those of ordinary skill.

Having fully described the invention, the following Examples are presented to exemplify but do not limit the invention.

Example 1:

21 g Propylene glycol, 5 g Monaquat® P-TL having the formula



16 g isopropyl alcohol, 1.5 g of 85 % [weight/volume] lactic acid, 1.1 g sodium chloride, and 0.11 g of hydroxy ethyl cellulose are dissolved in 55 ml of deionized water, and the pH is adjusted with 5 M NaOH to result in a solution of the invention having a pH of 5.0.

Example 2:

10.5 g Propylene glycol, 6 g Monaquat® P-TL (see example 1), 16 g isopropyl alcohol, 1.0 g tartaric acid, 1.0 g sodium chloride and 0.1 g HECQPTM 4400 (hydroxyethyl cellulose) are dissolved in 54 g of deionized water and the pH is adjusted to 5.0 with 5 M NaOH.

Examples 3 to 16:

The following examples are prepared according to example 1, except that the components set forth and in the amounts in the table below are used. Water is used to bring the total weight up to 100 g.

Ex.	Propylene glycol	Surfactant	Isopropyl Alcohol	Organic Acid	NaCl	HEC*	pH
3	10.5 g	Monaquat P-TL 6 g	16 g	Tartaric 1 g	0.5 g	0.1 g	5.5
4	20 g	Monaquat P-TL 6 g	16 g	Tartaric 1 g	0.5 g	0.1 g	5.5
5	10.5 g	Monaquat P-TL 6 g	16 g	Tartaric 1 g	0.5 g	-	5.5
6	30 g	Monaquat P-TL 6 g	16 g	Tartaric 1 g	0.5 g	-	5.5
7	30 g	Monaquat P-TL 6 g	8 g	Tartaric 1 g	0.5 g	-	5.5
8	30 g	Monaquat P-TL 6 g	8 g	Tartaric 1 g	0.5 g	-	5.0
9	30 g	Monaquat P-TL 6 g	16 g	Tartaric 1 g	0.5 g	0.1 g	5.5
10	10.5 g	Monaquat P-TL 6 g	8 g	Lactic 1.1 g	0.8 g	0.11 g	5.0
11	30 g	Monaquat P-TL 6 g	8 g	Tartaric 2 g	0.5 g	0.1 g	5.5
12	30 g	Monaquat P-TL 6 g	8 g	Lauric 0.0125 g	0.5 g	0.1 g	5.5
13	21 g	Monaquat P-TL 5 g	16 g	Lactic 1.5 g	1.1 g	0.11 g	5.0
14	20 g	Tween 20 20 g	16 g	Lactic 1.2 g	1.0 g	0.10 g	5.0
15	20 g	Triton X-100 2 g	16 g	Lactic 1.2 g	1.0 g	0.10 g	5.0
16	21.8 g	Tween 20 21.2 g	16.4 g	Lactic 1.47 g	1.0 g	-	5.0

* HEC = Hydroxyethyl Cellulose

Examples 17-20:

Examples 17-20 are prepared by dissolving in 49.3 g of water (deionized) isopropyl alcohol, propylene glycol and/or hexylene glycol as stated in the Table below. In addition, 1 g of Pluronic L-31 is dissolved therein. 2 g of lactic acid are added to result in a solution having a pH of 3.0.

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Example	Hexylene Glycol (g)	Isopropyl Alcohol (g)	Propylene Glycol (g)
17	30	40	0
18	30	30	10
19	20	40	10
20	10	50	10

Examples 21-24:

Examples 21-24 are prepared according to example 17 except that the Pluronic L-31 is replaced by 1.0 g of betaine and the following amounts of hexylene glycol, isopropyl alcohol, and propylene glycol are used.

Example	Hexylene Glycol (g)	Isopropyl Alcohol (g)	Propylene Glycol (g)
21	30	30	0
22	30	40	0
23	20	50	0
24	20	40	10

Example 25:

Solutions of the examples set forth below are tested for effectiveness against Acanthamoeba cysts as follows:

A 10^7 cyst pellet is dissolved in 10 ml of test solution to result in a 10^6 cyst/ml concentration in test solution. At the times specified below, 1 ml is withdrawn and diluted with 49 ml of saline to result in a cyst concentration of 2×10^4 cyst/ml. 0.1 ml of this diluted solution is then added to 10 ml of nutrient media so that the entire nutrient media begins with a 2×10^3 cyst population. The inoculated nutrient media are cultured for 3 weeks at which point effectiveness is assessed as (a) total kill (-) or (b) partial or no kill (+). The results are reported in the Table below.

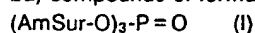
Solution Example No.	Exposure Time (min.)	
	1	5
17	+	-
18	+	-
19	+	-
20	+	-
21	+	-
22	+	-
23	+	-
24	+	-

Claims

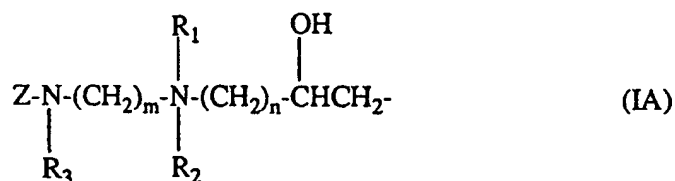
1. A disinfecting and cleaning composition comprising
- about 10 % by weight to about 50 % by weight of a C₃₋₈alkylene glycol;
 - about 0.5 % to about 25 % by weight of a compatible surfactant;
 - about 2 % to about 50 % by weight of a lower alkanol;
 - 0 to about 2 % by weight of a pH adjusting or regulating agent;
 - 0 up to an amount of a tonicity builder sufficient to raise the solution tonicity to less than the equivalent of a 5 % by weight NaCl solution;
 - 0 to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent;
- and
- the balance of a suitable solvent which is preferably water.

2. The composition of claim 1 wherein said surfactant is selected from

ba) compounds of formula I



wherein each group AmSur is independently of the formula



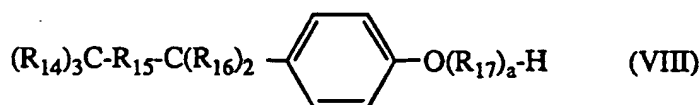
wherein each of R₁ and R₂ is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R₃ is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R₁ and R₂ is a carbon substituted by C₅₋₁₇alkyl; and n and m are each independently 1 to 4;

bb) compounds of the formula

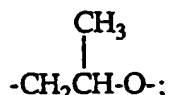


wherein R₉ is alkyl of 5-17 carbon atoms or a C₆₋₂₀alkanoylamino; each of R₁₀ and R₁₁ is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R₁₂ is an alpha,omega-alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R₁₃ is alpha,omega-C₁₋₅alkylene;

bc) compounds of the formula



wherein each R₁₄ and each R₁₆ is independently C₁₋₄alkyl; R₁₅ is C₁₋₄-alpha,omega-alkylene; each R₁₇ is independently -CH₂CH₂O-, -CH₂CH₂CH₂O-, or



and a is 3-18; and
bd) compounds of the formula



wherein B is a C_{1-4} -alpha,omega-alkylene; p is an integer from 0 to (d-1); b is an integer which is (d-p-1); d is 4 to 7; each R_{18} is independently H or a C_{1-4} alkyl which is unsubstituted or substituted by at least one R_{19} ; each R_{19} is independently hydroxy which is free, etherified by R_{20} , or esterified by R_{21} ; each R_{20} is a C_{2-4} straight or branched oxyalkylene or poly(C_{2-4} straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21} ; and each R_{21} is independently an acyl of a C_{2-24} alkanoic acid or a C_{4-24} alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group.

3. The composition of claim 1 which is a topical medicinal composition, a cosmetic, a facial cleanser, a surgical soap, a shampoo, a household disinfectant, or an industrial disinfectant.

4. The composition of claim 1 which is a contact lens polymer material cleaning and disinfecting solution comprising

- a) about 10 % by weight to about 50 % by weight of a C_{3-8} alkylene glycol;
 - b) about 0.5 % to about 25 % by weight of an ophthalmic device material compatible surfactant;
 - c) about 2 % to about 50 % by weight of a lower alkanol;
 - d) 0 to about 2 % by weight of a pH adjusting or regulating agent;
 - e) 0 up to an amount of a tonicity builder sufficient to raise the solution tonicity to less than the equivalent of a 5 % by weight NaCl solution;
 - f) 0 to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent;
- and

g) the balance of a suitable solvent which is preferably water.

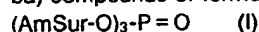
5. The solution of claim 4 comprising about 2 % to about 15 % by weight of said surfactant and about 2 % to about 30 % by weight of said alkanol.

6. The solution of claim 4 comprising

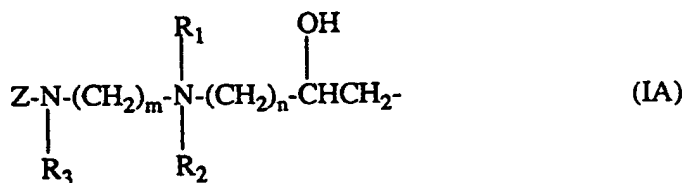
- a) about 10 % by weight to about 50 % by weight of a C_{3-8} alkylene glycol;
- b) about 0.5 % to about 25 % by weight of an ophthalmic device material compatible surfactant

selected from

ba) compounds of formula I

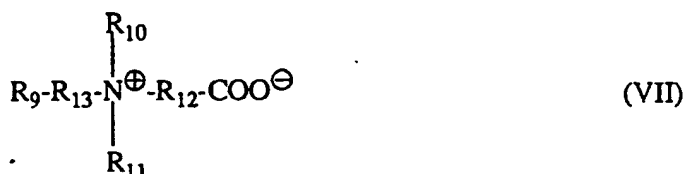


wherein each group AmSur is independently of the formula



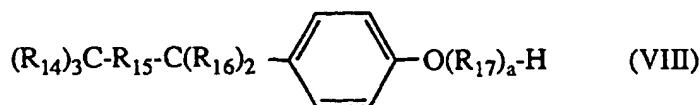
wherein each of R_1 and R_2 is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R_3 is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is an alkanoyl of 6-18 carbon atoms or Z together with R_1 and R_2 is a carbon substituted by C_{5-17} alkyl; and n and m are each independently 1 to 4;

bb) compounds of the formula

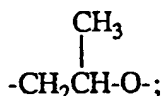


wherein R_9 is alkyl of 5-17 carbon atoms or a C_{6-20} alkanoylamino; each of R_{10} and R_{11} is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl; R_{12} is an α,ω -alkylene of 1 to 6 carbons which is unsubstituted or substituted by lower alkyl, hydroxy, or hydroxy lower alkyl; and R_{13} is α,ω - C_{1-5} alkylene;

bc) compounds of the formula



wherein each R_{14} and each R_{16} is independently C_{1-4} alkyl; R_{15} is C_{1-4} - α,ω -alkylene; each R_{17} is independently $-CH_2CH_2O-$, $-CH_2CH_2CH_2O-$, or



and a is 3-18; and

bd) compounds of the formula



wherein B is a C_{1-4} - α,ω -alkylene; p is an integer from 0 to $(d-1)$; b is an integer which is $(d-p-1)$; d is 4 to 7; each R_{18} is independently H or a C_{1-4} alkyl which is unsubstituted or substituted by at least one R_{19} ; each R_{19} is independently hydroxy which is free, etherified by R_{20} , or esterified by R_{21} ; each R_{20} is a C_{2-4} straight or branched oxyalkylene or poly(C_{2-4} straight or branched oxyalkylene), the terminal oxygen of which is bound to H or R_{21} ; and each R_{21} is independently an acyl of a C_{2-24} alkanoic acid or a C_{4-24} alkenoic acid; provided that in each compound of formula IX there is at least one free hydroxy group, and at least one R_{21} group;

poloxamers, reverse poloxamers, merxapols, poloxamines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, cetareths, NTA salts, EDTA salts, and pentetate salts;

c) about 2 % to about 50 % by weight of a lower alcohol;

d) 0 to about 2 % by weight of a pH adjusting or regulating agent selected from i) phosphoric acid, boric acid, lactic acid and citric acid, ii) an ophthalmically acceptable salt thereof, iii) a mixture of said acid and said salt of said acid, iv) an ophthalmically acceptable inorganic acid and v) an ophthalmically acceptable inorganic base;

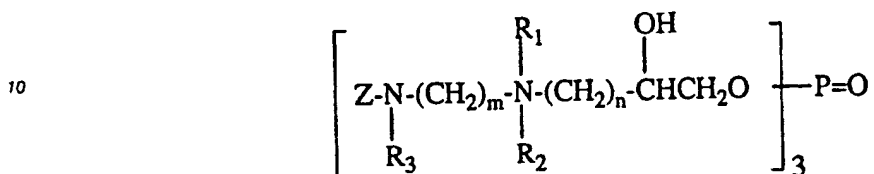
e) 0 to an amount of an ophthalmically acceptable alkali metal or alkaline earth metal halide, phosphate, carbonate or sulfate which is sufficient to raise the solution tonicity to less than the equivalent of a 5 % by weight sodium chloride solution;

f) 0 to an amount sufficient to bring the solution viscosity to 100 cps of a viscosity enhancing agent selected from hydroxy-lower alkyl-cellulose, hydroxy-lower alkanoyl cellulose, lower alkyl-cellulose, lower alkanoyl cellulose, carboxy-lower alkyl cellulose, poloxamers, reverse poloxamers, merxapols, polox-

amines, polyethyleneglycols, polypropyleneglycols, polypropyleneglycol-buteths, polypropyleneglycol oleates, polypropylene-pareths, tetrahydroxypropylethylenediamine, cetareths, NTA salts, EDTA salts, and pentetate salts and

g)water.

- 5 7. The solution of claim 4 wherein said C₃₋₈alkylene glycol is propylene glycol or hexylene glycol; said surfactant is of the formula



- 15 wherein each of R₁ and R₂ is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R₃ is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is C₆₋₁₈alkanoyl or Z, together with R₁ and R₂, is a carbon substituted by C₅₋₁₇alkyl, and n and m are each 1 to 4; in association with sufficient ions of counter charge to result in a net compound charge of zero;

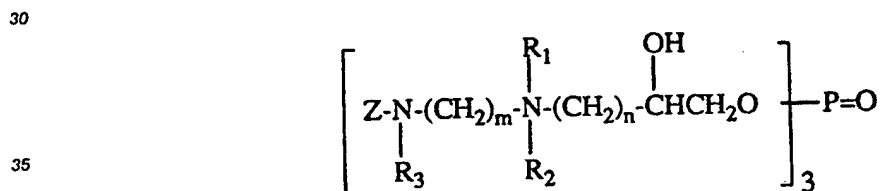
20 said lower alkanol is ethanol or isopropanol;

said pH adjusting or regulating agent is selected from i) phosphoric acid, boric acid, lactic acid and citric acid, ii) an ophthalmically acceptable salt thereof, iii) a mixture of said acid and said salt of said acid, iv) an ophthalmically acceptable inorganic acid and v) an ophthalmically acceptable inorganic base;

25 said tonicity builder is an ophthalmically acceptable alkali metal or alkaline earth metal halide, phosphate, carbonate or sulfate; and

said viscosity enhancer is selected from hydroxy-lower alkyl-cellulose, hydroxy-lower alkanoyl cellulose, lower alkyl-cellulose, lower alkanoyl cellulose and carboxy-lower alkyl cellulose.

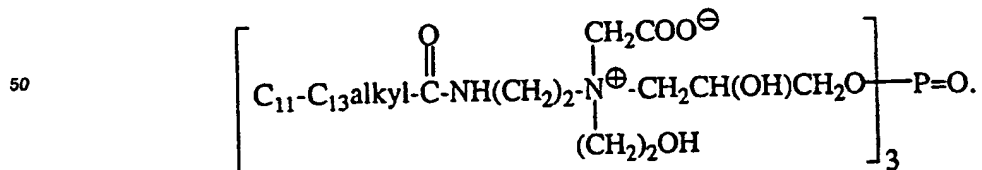
8. The solution of claim 6 wherein said C₃₋₈alkylene glycol is propylene glycol or hexylene glycol; said surfactant is of the formula



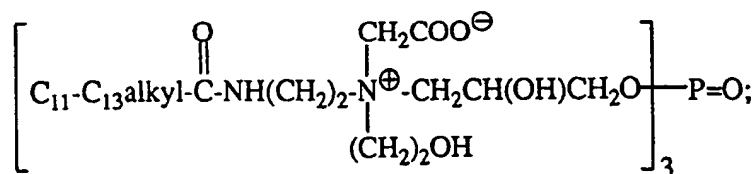
- 40 wherein each of R₁ and R₂ is independently lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, R₃ is hydrogen, lower alkyl, hydroxy lower alkyl, or carboxy lower alkyl, Z is C₆₋₁₈alkanoyl or Z, together with R₁ and R₂, is a carbon substituted by C₅₋₁₇alkyl, and n and m are each 1 to 4; in association with sufficient ions of counter charge to result in a net compound charge of zero;

said lower alkanol is ethanol or isopropanol; said pH adjusting agent is selected from hydrochloric and lactic acid; said tonicity builder is sodium chloride; and said viscosity enhancer is selected from poloxamer 407, poloxamer 101 and hydroxyethylcellulose.

45 9. The solution of claim 8 wherein said surfactant is of the formula



- 55 10. The solution of claim 4 wherein said C₃₋₈alkylene glycol is propylene glycol; said surfactant is of the formula



5 said lower alkanol is isopropyl alcohol; said pH adjusting or regulating agent is lactic acid; said tonicity
 10 builder is sodium chloride; and said viscosity enhancer is hydroxy ethyl cellulose.

11. The solution of claim 4 wherein said C₃₋₈alkylene glycol is present in an amount of about 21 % by
 weight; said surfactant is present in an amount of about 5 % by weight; said lower alkanol is present in an
 amount of about 16 % by weight; said pH adjusting or regulating agent is present in an amount of about 1.1
 % by weight; said tonicity builder is present in an amount of about 1 % by weight; and said viscosity
 15 enhancer is present in an amount of about 0.1 % by weight.

12. The solution of claim 4 comprising 0 to 30 % propylene glycol and/or 0 to 30 % hexylene glycol
 provided that the total amount of glycol is within the 50 % maximum as defined in claim 4, 0.5 to 8 % of
 Monaquat PTL or Pluronic L-31, 15 to 40 % isopropanol, 0 to 1.1 % sodium chloride and water.

13. A method of disinfecting and cleaning a contact lens polymer material comprising rubbing the
 20 surface of said polymer material with an effective disinfecting and cleaning amount of a solution of claim 4,
 followed by rinsing said polymer material with normal saline.

14. The method of claim 13 wherein each surface of said polymer material is rubbed with said solution
 for about 15 seconds and then the entire polymer material is rinsed with normal saline for about 10
 seconds.

25 15. The method of claim 14 wherein said polymer material is in the form of a contact lens.

16. The method of claim 14 wherein said rinsing step is followed by storing said polymer material in
 normal saline for about 1 minute.

17. Use of a composition according to any of claims 4 to 12 for disinfecting and cleaning a contact lens
 polymer material.

30 18. Method of manufacture of a composition of any of claims 4 to 12 characterized by convenient
 mixing of the individual components.

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(54) **Disinfecting and cleaning composition.**

(57) A rapid disinfecting formulation for ophthalmic devices, i.e. contact lenses inter alia, is disclosed. The formulations comprise a combination of a C₃₋₈alkylene glycol, an ophthalmically acceptable surfactant, a lower alkanol, water, and optionally a pH regulator, a tonicity enhancer, and a viscosity enhancer. The method comprises contacting the ophthalmic device to be disinfected with the above formulation, physically rubbing the device surface with the formulation, and rinsing the so treated device to remove remaining residue.

EP 0 381 618 A3



European
Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 81 0049

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	US-A-3 694 365 (CH. C. CASTNER) * the whole document ** - - - -	1,3	A 61 L 2/00 C 11 D 3/00 C 11 D 3/20
X	FR-A-2 406 439 (E.B. MICHAELS) * page 3, line 32 - line 38; claims; examples ** - - - -	1,2,3	
X	GB-A-718 050 (MILES LAB.) * the whole document ** - - - -	1,3	
A	EP-A-0 233 842 (CIBA-GEIGY) * claims ** - - - -	1	
A	EP-A-0 209 192 (ICN) * claims ** - - - - -	1	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 L C 11 D
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of search 18 December 91	Examiner GOLLER P.
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